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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/697,703

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H. William Bosch

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EXAMINER

MAHYERA, TRISTAN J

ART UNIT

PAPER NUMBER

1615

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/697,703	Applicant(s) BOSCH ET AL.	
	Examiner TRISTAN J. MAHYERA	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31,36-38,40 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31,36-38,40 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/05/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of Amendments and Remarks, filed 1/04/08, is acknowledged. Claims 1-31, 36-38, 40 and 44 are pending. Claims 1-3, 13, 17, 22, 23, 27-31 and 37 were amended. Claims 32-35, 39, 41-43 were withdrawn.

Claim Objections

Objection of Claim 27 is **withdrawn** in light of Applicant's amendment.

Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 1-18, 20, 22-31, 36, 37, 38, 40 and 44 in the action filed 9/05/07, is **withdrawn** in light of Applicant's amendments.

The following rejections are **maintained** and elaborated upon.

Claims 19 and 21 **remain** rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 21 use the terms "at least" and "about" to describe the Cmax and AUC, which does not particularly point out and distinctly claim the subject matter. Taking into consideration Applicant's definition of "about" as plus or minus 10% (see

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page 10 and 11 paragraph [0030]) which gives a range of 9.9% to 110% the use of “at least” renders the claim indefinite because it is unclear if Applicant is trying to claim at least 9.9%, at least 110% or somewhere within the range 9.9% to 110%.

Claim Rejections - 35 USC § 102

The text of the 35 USC § 102 not included in this action can be found in a prior Office Action.

Claims 1-14 and 27-31 **remain** rejected under 35 U.S.C. 102(e) as being anticipated by OLIVIERI et al (WO 2005/000273) for reasons of record and those discussed below in the response.

Response to Arguments

Applicant's arguments have been fully considered, but are not found persuasive.

Applicants argue that no reasonable conclusion as to the inherent teachings of OLIVIERI can be made because of two seemingly incongruent statements. The first is "the use of linear copolymer N-vinyl-2-pyrrolidone/vinyl acetate as carrier for co-grinding of scarcely water soluble drugs results in improvements of the crystalline structure of said drugs (reduction of melting enthalpy and/or melting point)". The second statement is "NVP/VA has a clearly higher ability in de-structuring nimesulide (lower melting enthalpies and temperature)". This argument is not found persuasive because under 35 USC § 102, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

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Verdegaal Bros. v. Union oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). In the instant case, the limitation of claim 1 argued by the Applicant as not being anticipated is “(b) at least one surface stabilizer adsorbed on the surface of the particles.”, and specifically directed to the point that OLIVIERI is silent about the stabilizer being adsorbed by the nimesulide particles. A preferred surface stabilizer according to the instant invention is the copolymer of vinyl acetate and vinyl pyrrolidone (NVP/VA), see e.g. instant claim 14. The OLIVIERI reference exemplifies a composition of nimesulide and this specific copolymer, NVP/VA. See e.g. Examples 1-4. “Products of identical chemical composition can not have mutually exclusive properties.’ A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).” See MPEP 2112.01. In this case, the identical structural components (nimesulide and NVP/VA) are taught, thus the same adsorbing properties must be present.

Claim Rejections - 35 USC § 103

The test of those sections of 35 USC § 103 not included in this section can be found in a prior Office Action.

Applicant's traverse of the 35 USC § 103 rejections have been considered, but are found moot in view of following **new** rejections necessitated by amendment.

Claims 1 10-13 and 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of LIVERSIDGE et al. (US 5,552,160 see PTO-1449 filed 4/01/2004).

OLIVIERI teaches a nimesulide and carrier composition to improve *inter alia* dissolution and solubility profiles, as described above.

OLIVIERI does not exemplify any Tmax, Cmax or AUC profile of nimesulide.

LIVERSIDGE teaches that nanoparticles of NSAIDs having a surface modifier adsorbed on the surface hasten onset of the active. See e.g. col 1 lines 61-64. The reference teaches nanoparticles have decreased Tmax, increased Cmax and increased AUC when compared to non-nanoparticles. See e.g. col 9 lines 1-20; instant claims 16-21 and 25-26. The size of the control was between 20-30 microns (see col 7 lines 35-38) while the size of the nanoparticles was between 240-300nm (see col 7 lines 32-34); instant claims 16-21 and 25-26. The composition is considered bioadhesive because the surface modifiers physically adhere to the surface of the NSAID but do not chemically bond to the NSAID. See e.g. col 3 lines 25-27; instant claim 15. LIVERSIDGE further teaches a simple screening process to determine compatible surface modifies with NSAIDs and also the amounts of surface modifier and NSAID can be adjusted by known variables. See e.g. col 6 lines 16-55 and col 6 lines 5-15.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make a composition comprising nanoparticles of nimesulide and a surface stabilizer that decreases the Tmax and increases the Cmax and AUC of nimesulide compared to non-nanoparticles, as taught by OLIVIERI in view of

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LIVERSIDGE. One of ordinary skill in the art at the time the invention was made would have been motivated to combine these elements into a single composition because of the beneficial effects of hastening the onset of the NSAID, improving dissolution and reducing side effects, as taught by LIVERSIDGE. Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention.

Instant Claims 1, 36-38 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of SINGH et al. (Analytical Profiles of Drug Substances and Excipients, Volume 28, 2001, p197-249) and in view of MERCK (The Merck Index 12th ed. Merck & Co. 1996, codeine, p416-417).

OLIVIERI teaches a nimesulide and carrier composition to improve *inter alia* dissolution and solubility profiles, as described above. OLIVIERI further teaches using analgesics as the active substance in the composition, but does not teach adding additional specific analgesics to the composition. See Table 1 and 6, page 10 lines 31-33, page 5 line 5 to page 6 line 9 and claim 15.

OLIVIERI does not teach the further addition of a non-nimesulide active agent, such as analgesics, specifically codeine.

SINGH et al. teaches it is well known in the art that nimesulide has anti-inflammatory and analgesic properties. See section 1.5. It is also well known in the art that codeine has analgesic properties as shown in MERCK. Furthermore, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be

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useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Thus, the addition of codeine, an analgesic, would be obvious to someone of skill in the art at the time of the invention because nimesulide also has known analgesic properties, resulting in the practice of the instantly claimed invention with a reasonable expectation of success; instant claims 36-38 and 40.

Instant Claims 1 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over OLIVIERI et al. (WO 2005/000273) in view of BUHL et al. (US 5,776,563 see PTO-892 filed 9/05/2007).

OLIVIERI teaches a nimesulide and carrier composition to improve *inter alia* dissolution and solubility profiles, as described above. OLIVIERI further teaches that a composition administered to a subject must be free of microorganisms. See page 6 lines 26-28.

OLIVIERI does not exemplify that the composition is sterile filtered.

BUHL teaches that pharmaceutical compositions can be sterilized by conventional sterilization techniques or may be sterile filtered. See column 4 lines 7-26; instant claim 44. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to sterile filter a nimesulide and surface stabilizer composition, as taught by OLIVIERI in view of BUHL. One of ordinary skill in the art at the time the invention was made would have been motivated to destroy any

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microorganisms by sterile filtering the composition, as taught by BUHL. Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TRISTAN J. MAHYERA whose telephone number is 571-270-1562. The examiner can normally be reached on Monday through Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL P. WOODWARD can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

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/Tristan J Mahyera/
Examiner, Art Unit 1615

/Michael P Woodward/
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